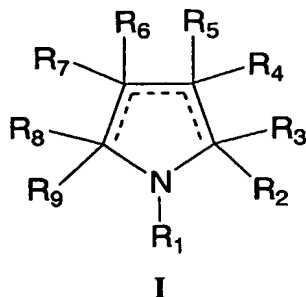


WHAT IS CLAIMED IS:

1. A compound of Formula I:



or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

a is 0 or 1;

10 b is 0 or 1;

m is 0, 1, or 2;

r is 0 or 1;

s is 0 or 1; and

u is 2, 3, 4 or 5;

15 a dashed line represents an optional double bond, provided that one and only one double bond is present in the ring;

R¹ is selected from:

- 20 1) (C=O)O-C₁-C₁₀ alkyl,
 2) (C=O)O-aryl,
 3) (C=O)O-C₂-C₁₀ alkenyl,
 4) (C=O)O-C₂-C₁₀ alkynyl,
 5) (C=O)O-C₃-C₈ cycloalkyl, and
 25 6) (C=O)O-heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R² and R⁶ are independently selected from:

- 1) aryl,
- 2) C₁-C₆ aralkyl,
- 3) C₃-C₈ cycloalkyl, and
- 5 4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

10 provided that R² and R⁶ are not both an unsubstituted aryl selected from phenyl and naphthyl;

R³, R⁴, R⁵, R⁷, R⁸, and R⁹ are independently selected from:

- 1) H,
- 2) C₁-C₁₀ alkyl,
- 15 3) aryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) C₁-C₆ perfluoroalkyl,
- 7) C₁-C₆ aralkyl,
- 20 8) C₃-C₈ cycloalkyl, and
- 9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰; or

25 R⁴ and R⁵, or R⁸ and R⁹, attached to the same carbon atom are combined to form -(CH₂)_u- wherein one of the carbon atoms is optionally replaced by a moiety selected from O, S(O)_m, -N(R^a)C(O)-, -N(R^b)- and -N(COR^a)-;

R¹⁰ is independently selected from:

- 30 1) (C=O)_aO_bC₁-C₁₀ alkyl,
- 2) (C=O)_aO_baryl,
- 3) C₂-C₁₀ alkenyl,
- 4) C₂-C₁₀ alkynyl,
- 5) (C=O)_aO_b heterocyclyl,

- 6) CO_2H ,
 7) halo,
 8) CN ,
 9) OH ,
 5 10) $\text{O}_b\text{C}_1\text{-C}_6$ perfluoroalkyl,
 11) $\text{O}_a(\text{C}=\text{O})_b\text{NR}^{12}\text{R}^{13}$,
 12) $\text{S}(\text{O})_m\text{R}^a$,
 13) $\text{S}(\text{O})_2\text{NR}^{12}\text{R}^{13}$,
 14) oxo,
 10 15) CHO ,
 16) $(\text{N}=\text{O})\text{R}^{12}\text{R}^{13}$, and
 17) $(\text{C}=\text{O})_a\text{O}_b\text{C}_3\text{-C}_8$ cycloalkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R^{11} ;

15

R^{11} is selected from:

- 1) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_1\text{-C}_{10})\text{alkyl}$,
 2) $\text{O}_r(\text{C}_1\text{-C}_3)\text{perfluoroalkyl}$,
 3) $(\text{C}_0\text{-C}_6)\text{alkylene-S}(\text{O})_m\text{R}^a$,
 20 4) oxo,
 5) OH ,
 6) halo,
 7) CN ,
 8) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkenyl}$,
 25 9) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_2\text{-C}_{10})\text{alkynyl}$,
 10) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_3\text{-C}_6)\text{cycloalkyl}$,
 11) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_0\text{-C}_6)\text{alkylene-aryl}$,
 12) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_0\text{-C}_6)\text{alkylene-heterocyclyl}$,
 13) $(\text{C}=\text{O})_r\text{O}_s(\text{C}_0\text{-C}_6)\text{alkylene-N}(\text{R}^b)_2$,
 30 14) $\text{C}(\text{O})\text{R}^a$,
 15) $(\text{C}_0\text{-C}_6)\text{alkylene-CO}_2\text{R}^a$,
 16) $\text{C}(\text{O})\text{H}$,
 17) $(\text{C}_0\text{-C}_6)\text{alkylene-CO}_2\text{H}$,
 18) $\text{C}(\text{O})\text{N}(\text{R}^b)_2$,

19) $S(O)_m R^a$, and

20) $S(O)_2 N(R^b)_2$

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH, (C_1-C_6) alkoxy,

5 halogen, CO_2H , CN, $O(C=O)C_1-C_6$ alkyl, oxo, and $N(R^b)_2$;

R^{12} and R^{13} are independently selected from:

- 1) H,
- 2) $(C=O)O_b C_1-C_{10}$ alkyl,
- 10 3) $(C=O)O_b C_3-C_8$ cycloalkyl,
- 4) $(C=O)O_b$ aryl,
- 5) $(C=O)O_b$ heterocyclyl,
- 6) C_1-C_{10} alkyl,
- 7) aryl,
- 15 8) C_2-C_{10} alkenyl,
- 9) C_2-C_{10} alkynyl,
- 10) heterocyclyl,
- 11) C_3-C_8 cycloalkyl,
- 12) $SO_2 R^a$, and
- 20 13) $(C=O)NR^b_2$,

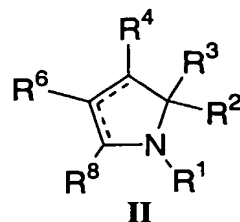
said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R^{11} , or

25 R^{12} and R^{13} can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R^{11} ;

30 R^a is (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, aryl, or heterocyclyl; and

R^b is H, (C_1-C_6) alkyl, aryl, heterocyclyl, (C_3-C_6) cycloalkyl, $(C=O)OC_1-C_6$ alkyl, $(C=O)C_1-C_6$ alkyl or $S(O)_2 R^a$.

2. A compound of the Formula II,



5 or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

a is 0 or 1;

b is 0 or 1;

m is 0, 1, or 2;

10 r is 0 or 1;

s is 0 or 1;

a dashed line represents an optional double bond, provided that one and only one double bond is present in the ring;

15

R¹ is selected from:

- 1) (C=O)O-C₁-C₁₀ alkyl,
- 2) (C=O)O-aryl,
- 3) (C=O)O-C₂-C₁₀ alkenyl,
- 20 4) (C=O)O-C₂-C₁₀ alkynyl,
- 5) (C=O)O-C₃-C₈ cycloalkyl, and
- 6) (C=O)O-heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

25

R² and R⁶ are independently selected from:

- 1) aryl,
- 2) C₁-C₆ aralkyl,
- 3) C₃-C₈ cycloalkyl, and

4) heterocyclyl,
said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

5 provided that R² and R⁶ are not both an unsubstituted aryl selected from phenyl and naphthyl;

R³, R⁴ and R⁸ are independently selected from:

- 1) H,
- 10 2) C₁-C₁₀ alkyl,
- 3) aryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) C₁-C₆ perfluoroalkyl,
- 15 7) C₁-C₆ aralkyl,
- 8) C₃-C₈ cycloalkyl, and
- 9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

20

R¹⁰ is independently selected from:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl,
- 2) (C=O)_aO_baryl,
- 3) C₂-C₁₀ alkenyl,
- 25 4) C₂-C₁₀ alkynyl,
- 5) (C=O)_aO_b heterocyclyl,
- 6) CO₂H,
- 7) halo,
- 8) CN,
- 30 9) OH,
- 10) O_bC₁-C₆ perfluoroalkyl,
- 11) O_a(C=O)_bNR¹²R¹³,
- 12) S(O)_mR^a,
- 13) S(O)₂NR¹²R¹³,
- 35 14) oxo,

- 15) CHO,
- 16) (N=O)R¹²R¹³, and
- 17) (C=O)_aO_bC₃-C₈ cycloalkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted
 5 with one, two or three substituents selected from R¹¹;

R¹¹ is selected from:

- 1) (C=O)_rO_s(C₁-C₁₀)alkyl,
- 2) O_r(C₁-C₃)perfluoroalkyl,
- 10 3) oxo,
- 4) OH,
- 5) halo,
- 6) CN,
- 7) (C₂-C₁₀)alkenyl,
- 15 8) (C₂-C₁₀)alkynyl,
- 9) (C=O)_rO_s(C₃-C₆)cycloalkyl,
- 10) (C=O)_rO_s(C₀-C₆)alkylene-aryl,
- 11) (C=O)_rO_s(C₀-C₆)alkylene-heterocyclyl,
- 12) (C=O)_rO_s(C₀-C₆)alkylene-N(R^b)₂,
- 20 13) C(O)R^a,
- 14) (C₀-C₆)alkylene-CO₂R^a,
- 15) C(O)H,
- 16) (C₀-C₆)alkylene-CO₂H,
- 17) C(O)N(R^b)₂,
- 25 18) S(O)_mR^a, and
- 19) S(O)₂N(R^b)₂;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

30

R¹² and R¹³ are independently selected from:

- 1) H,
- 2) (C=O)O_bC₁-C₁₀ alkyl,
- 3) (C=O)O_bC₃-C₈ cycloalkyl,

- 4) (C=O)O_baryl,
 5) (C=O)O_bheterocyclyl,
 6) C₁-C₁₀ alkyl,
 7) aryl,
 5 8) C₂-C₁₀ alkenyl,
 9) C₂-C₁₀ alkynyl,
 10) heterocyclyl,
 11) C₃-C₈ cycloalkyl,
 12) SO₂R^a, and
 10 13) (C=O)NR^b₂,

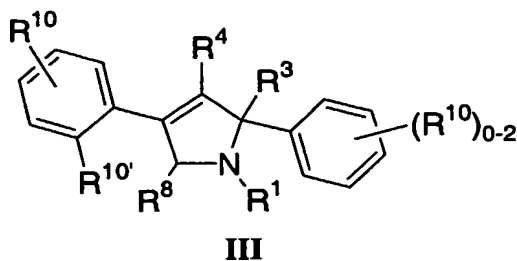
said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R¹¹, or

- R¹² and R¹³ can be taken together with the nitrogen to which they are attached to
 15 form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

- 20 R^a is (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl; and

R^b is H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆alkyl, (C=O)C₁-C₆alkyl or S(O)₂R^a.

- 25 3. The compound according to Claim 2 of the formula III:



or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

- a is 0 or 1;
 b is 0 or 1;
 5 m is 0, 1, or 2;
 r is 0 or 1;
 s is 0 or 1;

R¹ is selected from:

- 10 1) (C=O)O-C₁-C₁₀ alkyl,
 2) (C=O)O-aryl,
 3) (C=O)O-C₃-C₈ cycloalkyl, and
 4) (C=O)O-heterocyclyl,

15 said alkyl, aryl, cycloalkyl, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R³, R⁴ and R⁸ are independently selected from:

- 1) H,
 2) C₁-C₁₀ alkyl, and
 20 3) C₁-C₆ perfluoroalkyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R¹⁰ is independently selected from:

- 25 1) (C=O)_aO_bC₁-C₁₀ alkyl,
 2) (C=O)_aO_baryl,
 3) C₂-C₁₀ alkenyl,
 4) C₂-C₁₀ alkynyl,
 5) (C=O)_aO_b heterocyclyl,
 30 6) CO₂H,
 7) halo,
 8) CN,
 9) OH,
 10) O_bC₁-C₆ perfluoroalkyl,
 35 11) O_a(C=O)_bNR¹²R¹³,

- 12) $S(O)_m R^a$,
 13) $S(O)_2 N R^{12} R^{13}$,
 14) oxo,
 15) CHO,
 5 16) $(N=O) R^{12} R^{13}$, and
 17) $(C=O)_a O_b C_3-C_8$ cycloalkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R^{11} ;

10 $R^{10'}$ is halogen;

R^{11} is selected from:

- 1) $(C=O)_r O_s (C_1-C_{10})$ alkyl,
 2) $O_r (C_1-C_3)$ perfluoroalkyl,
 15 3) oxo,
 4) OH,
 5) halo,
 6) CN,
 7) (C_2-C_{10}) alkenyl,
 20 8) (C_2-C_{10}) alkynyl,
 9) $(C=O)_r O_s (C_3-C_6)$ cycloalkyl,
 10) $(C=O)_r O_s (C_0-C_6)$ alkylene-aryl,
 11) $(C=O)_r O_s (C_0-C_6)$ alkylene-heterocyclyl,
 12) $(C=O)_r O_s (C_0-C_6)$ alkylene- $N(R^b)_2$,
 25 13) $C(O) R^a$,
 14) (C_0-C_6) alkylene- $CO_2 R^a$,
 15) $C(O) H$,
 16) (C_0-C_6) alkylene- $CO_2 H$,
 17) $C(O) N(R^b)_2$,
 30 18) $S(O)_m R^a$, and
 19) $S(O)_2 N(R^b)_2$;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

5 R¹² and R¹³ are independently selected from:

- 1) H,
- 2) (C=O)O_bC₁-C₁₀ alkyl,
- 3) (C=O)O_bC₃-C₈ cycloalkyl,
- 4) (C=O)O_baryl,
- 10 5) (C=O)O_bheterocyclyl,
- 6) C₁-C₁₀ alkyl,
- 7) aryl,
- 8) C₂-C₁₀ alkenyl,
- 9) C₂-C₁₀ alkynyl,
- 15 10) heterocyclyl,
- 11) C₃-C₈ cycloalkyl,
- 12) SO₂R^a, and
- 13) (C=O)NR^b₂.

20 said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R¹¹, or

R¹² and R¹³ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms
 25 selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^a is independently selected from: (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, and heterocyclyl; and

30

R^b is independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl or S(O)₂R^a.

~~3.~~

The compound according to Claim 3 of the formula III, or the pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

5

R¹ is (C=O)O-C₁-C₁₀ alkyl,

said alkyl, is optionally substituted with one, two or three substituents selected from R¹⁰;

10 R³, R⁴ and R⁸ are independently selected from:

- 1) H, and
- 2) C₁-C₁₀ alkyl,

said alkyl is optionally substituted with one or more substituents selected from R¹⁰; and

15

R¹⁰, R¹¹, R¹², R¹³, R^a and R^b are as described in Claim 3.

5. A compound selected from:

20 methyl 4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

allyl 4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

ethyl 4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

25

phenyl 4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

isopropyl 4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

30 2-(dimethylamino)-2-methylpropyl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

2-aminoethyl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

35

3-aminopropyl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

40

pyrrolidin-3-yl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate;

piperidin-4-yl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate;

5 or a pharmaceutically acceptable salt or stereoisomer thereof.

6. The compound according to Claim 5 which is the TFA salt of a compound selected from:

10 2-(dimethylamino)-2-methylpropyl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate;

2-aminoethyl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate;

15 3-aminopropyl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate;

20 pyrrolidin-3-yl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate; and

piperidin-4-yl (2*S*)-4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate.

25 7. A pharmaceutical composition that is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

8. A method of treating or preventing cancer in a mammal in need of such treatment that is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1.

9. A method of treating cancer or preventing cancer in accordance with Claim 8 wherein the cancer is selected from cancers of the brain, genitourinary tract, lymphatic system, stomach, larynx and lung.

35 10. A method of treating or preventing cancer in accordance with Claim 8 wherein the cancer is selected from histiocytic lymphoma, lung

adenocarcinoma, small cell lung cancers, pancreatic cancer, glioblastomas and breast carcinoma.

11. A process for making a pharmaceutical composition which
5 comprises combining a compound of Claim 1 with a pharmaceutically acceptable carrier.

12. The composition of Claim 7 further comprising a second compound selected from:

- 10 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,
- 3) a retinoid receptor modulator,
- 4) a cytotoxic/cytostatic agent,
- 5) an antiproliferative agent,
- 15 6) a prenyl-protein transferase inhibitor,
- 7) an HMG-CoA reductase inhibitor,
- 8) an HIV protease inhibitor,
- 9) a reverse transcriptase inhibitor,
- 10) an angiogenesis inhibitor, and
- 20 11) a PPAR- γ agonist,
- 12) a PPAR- δ agonists;
- 13) an inhibitor of cell proliferation and survival signaling, and
- 14) an agent that interferes with a cell cycle checkpoint.

25 13. The composition of Claim 12, wherein the second compound is an angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP inhibitor, an integrin blocker, interferon- α , interleukin-12, pentosan polysulfate, a
30 cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-(chloroacetyl-carbonyl)-fumagillol, thalidomide, angiostatin, troponin-1, and an antibody to VEGF.

14. The composition according to Claim 7 further comprising a
35 proteasome inhibitor.

15. The composition according to Claim 7 further comprising a
aurora kinase inhibitor.
- 5 16. The composition according to Claim 7 further comprising a Raf
kinase inhibitor.
17. The composition according to Claim 7 further comprising a
serine/threonine kinase inhibitor.
- 10 18. The composition according to Claim 7 further comprising an
inhibitor of another mitotic kinesin which is not KSP.
19. The composition of Claim 12, wherein the second compound is
15 an estrogen receptor modulator selected from tamoxifen and raloxifene.
20. A method of treating cancer which comprises administering a
therapeutically effective amount of a compound of Claim 1 in combination with
radiation therapy.
- 20 21. A method of treating or preventing cancer that comprises
administering a therapeutically effective amount of a compound of Claim 1 in
combination with a compound selected from:
- 25 1) an estrogen receptor modulator,
2) an androgen receptor modulator,
3) a retinoid receptor modulator,
4) a cytotoxic/cytostatic agent,
5) an antiproliferative agent,
6) a prenyl-protein transferase inhibitor,
30 7) an HMG-CoA reductase inhibitor,
8) an HIV protease inhibitor,
9) a reverse transcriptase inhibitor,
10) an angiogenesis inhibitor,
11) PPAR- γ agonists,
35 12) PPAR- δ agonists,

- 13) an inhibitor of inherent multidrug resistance,
14) an anti-emetic agent,
15) an agent useful in the treatment of anemia,
16) an agent useful in the treatment of neutropenia,
5 17) an immunologic-enhancing drug,
18) an inhibitor of cell proliferation and survival signaling, and
19) an agent that interferes with a cell cycle checkpoint.

22. A method of treating cancer that comprises administering a
10 therapeutically effective amount of a compound of Claim 1 in combination with
radiation therapy and a compound selected from:

- 1) an estrogen receptor modulator,
2) an androgen receptor modulator,
3) a retinoid receptor modulator,
15 4) a cytotoxic/cytostatic agent,
5) an antiproliferative agent,
6) a prenyl-protein transferase inhibitor,
7) an HMG-CoA reductase inhibitor,
8) an HIV protease inhibitor,
20 9) a reverse transcriptase inhibitor,
10) an angiogenesis inhibitor,
11) PPAR- γ agonists,
12) PPAR- δ agonists,
13) an inhibitor of inherent multidrug resistance,
25 14) an anti-emetic agent,
15) an agent useful in the treatment of anemia,
16) an agent useful in the treatment of neutropenia,
17) an immunologic-enhancing drug,
18) an inhibitor of cell proliferation and survival signaling, and
30 19) an agent that interferes with a cell cycle checkpoint.

23. A method of treating or preventing cancer which comprises
administering a therapeutically effective amount of a compound of Claim 1 and
paclitaxel or trastuzumab.

35

24. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 and a GPIIb/IIIa antagonist.
- 5 25. The method of Claim 33 wherein the GPIIb/IIIa antagonist is tirofiban.
26. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in
10 combination with a COX-2 inhibitor.
27. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a proteasome inhibitor.
15
28. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with an aurora kinase inhibitor.
- 20 29. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a Raf kinase inhibitor.
30. A method of treating or preventing cancer which comprises
25 administering a therapeutically effective amount of a compound of Claim 1 in combination with a serine/threonine kinase inhibitor.
31. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in
30 combination with an inhibitor of a mitotic kinesin that is not KSP.
32. A method of modulating mitotic spindle formation which comprises administering a therapeutically effective amount of a compound of Claim
1.
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33. A method of inhibiting the mitotic kinesin KSP which comprises administering a therapeutically effective amount of a compound of Claim 1.